UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,874	02/06/2001	Iris Pecker	01/21603	8407

7590 04/02/2007

Martin D. Moynihan
PRTSI, Inc.
P. O. Box 16446
Arlington, VA 22215

EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/776,874	PECKER ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *97-101 and 127-133* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97-101 and 130-133* is/are rejected.

7)☒ Claim(s) *127-129* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/1/2007 has been entered.

Applicant's amendment of claim 128, cancellation of claims 123-126 and the addition of new claims 130-133, in the paper of 2/1/2007, is acknowledged.

Claims 97-101 and 127-133 are at issue and are present for examination.

Applicants' arguments filed on 2/1/2007 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 100, 101, 127, 128 is objected to because of the following informalities:

Claims 100, 101, 127, 128 are dependent on rejected claim 97.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 97-99 and 130-133 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein or preparation comprising said protein having the amino acid sequence of SEQ ID NO: 10, said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, does not reasonably provide enablement for any protein or preparation comprising said protein having heparanase activity or being so cleavable so as to acquire said heparanase activity, wherein said protein is merely 70% homologous to SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was originally stated in the previous office actions as it applied to previous claims 97-99 and 123-126. In response to that rejection applicants amended claims 97, 123, 125, canceled of claims 119-122 and added new claims 128 and 129 and traverse the rejection as it applies to the new claims. The rejection was maintained in the final office action as it applied to claims 97-99 ad 123-126. In response to this rejection applicants have cancelled claims 123-126 and added new claims 130-133 and

traverse this rejection as it applies to the claims. Claims 130-133 are included in the rejection for the reasons previously stated for claim 97 from which they depend.

Applicants continue to traverse the rejection on the basis that the decision of the Board of Patent Appeals and Interferences in *Ex Parte Sun* dictates a finding of enablement in the instant invention. Applicants comments are acknowledged and applicants are reminded that the referred to case was not written for publication and is not binding precedent of the Board.

Applicants submit that the office action fails to make a single substantive point in comparing the subject claims to that of Sun and that the allegation that applicants have not compared the subject case to Sun beyond the percent homology claimed is completely untrue. Applicants submit that the chemical nature of the compounds claimed here and in *Sun*, how to screen for activity and how to vary the claimed compound of the subject claims and in *Sun* are each disclosed and applicants attempts to support each of applicants points.

As was previously stated, the factors necessary for the determination of the enablement of the instant claims and that of the referred to board decision are different. For applicants convenience it is pointed out to applicants that the referred to claims from *Ex parte Sun* are drawn to a wee1 'polynucleotide' having at least 80% identity to the entire coding region of SEQ ID NO: 1 and this is a 403 amino acid encoding polynucleotide. The instant claims are drawn to a "preparation comprising a heparanase protein" said heparanase having at least 70% homology to SEQ ID NO: 10, wherein said heparanase is pure enough to elicit anti-heparanase antibodies.

While the examiner has not presented an exhaustive list comparing each of the Wands factors for the instant claims and that of Ex parte Sun, applicants have neither pointed out similarities between the two decisions beyond that the each encompasses a percent homology or identity and a protein or polynucleotide. Applicants continue to submit that beyond the chemical nature of the claimed compounds, applicants and Sun each disclose how to vary and how to screen for activity of the compounds being claimed. Applicant's complete argument regarding the Ex parte Sun decision continues to be acknowledged, and as has been previously stated, the facts of the Sun case and the facts of the instant application while similar are different. Applicants pointing out of similarities between the two cases is acknowledged, however, the pointed out similarities are not considered to be persuasive in supporting applicants argument, because the pointed out similarities are but a few of the factors considered in making any decision regarding enablement and the examiner sees many more differences than similarities.

As has been previously stated, the factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

With respect to the nature of the invention, as previously stated, the referred to claims from *Ex parte Sun* are drawn to a wee1 'polynucleotide' having at least 80% identity to the entire coding region of SEQ ID NO: 1 and this is a 403 amino acid encoding polynucleotide. The instant claims are drawn to a "preparation" not a polynucleotide, comprising a heparanase protein said heparanase having at mere 70% homology to SEQ ID NO: 10 a 543 amino acid protein, said preparation being pure enough to elicit anti-heparanase antibodies.

Further the state of the prior art with respect to preparations comprising the claimed heparanase able to elicit anti-heparanase antibodies, is considerably different than prior art comprising polynucleotides which encode a wee1 polynucleotide.

The skill in the art regarding the screening and isolation of a polynucleotide encoding a wee1 protein and producing a preparation comprising a heparanase protein homologous to SEQ ID NO: 10 wherein said preparation is pure enough to elicit anti-heparanase antibodies is clearly different, and the direction and guidance necessary to obtain these clearly different inventions is also very different.

As previously stated on the record, the specification does not support the broad scope of the claims which encompass the claimed preparations comprising a heparanase protein, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting heparanase activity; (B) the general tolerance of heparanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a heparanase with an expectation of obtaining the desired biological function; and (D) the specification

provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the heparanase activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of the claimed genus.

Applicants submit that there are three objective scientific reasons why the skilled artisan could have identified working embodiments that fall within the scope of claims 97-99 with routine experimentation. Applicants submit that genetic drift or variation within the naturally occurring species of heparanase proteins provides a roadmap for variations including point mutations. Applicants submit that the skilled artisan's knowledge of protein chemistry allows prediction of preserved biological properties so long as amino acid substitutions are conservative in their nature and the secondary structure of heparanase, would allow the skilled artisan to predict areas of non-criticality where even non-conservative substitutions may be introduced. Applicants refer to the comparative analysis of the amino acid sequence of different species of heparanase and the secondary structure of heparanase protein in making these assertions.

Applicants complete argument is further acknowledged, however, continues to not be found persuasive on the following basis. With respect to applicants assertion that genetic drift or variation within the naturally occurring species of heparanase proteins provides a roadmap for variations including point mutations, this roadmap is not

sufficient to enable the claimed scope of heparanase proteins encompassed by the claims and the level of skill in the art of protein chemistry is not sufficient to fill in that necessary guidance needed to enable such a broadly claimed genus.

As previously stated, current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would not allow for finding the few active mutants within the several hundred thousand to greater then several trillions of inactive mutants, as is the case for the claims limited to 70% identity. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any heparanase having a mere 70% homology to SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those preparations having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 97-101 and 130-133 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuks et al. (U.S. Patent No. 5,362,641).

The rejection was originally stated in the previous office action of 10/3/2005 as it applied to previous claims 97-101 and 119-127. The rejection was maintained over claims 97-101 and 123-126 in the office action of 11/1/2006. In response to this rejection applicants have canceled claims 123-126 and added new claims 130-133 and traverse the rejection as it applies to the new claims. Claims 130-133 are included in the rejection for the reasons previously stated for claim 97 from which they depend.

Applicants continue to argue on the basis that the preparation of Fuks et al. cannot or does not elicit antibodies against heparanase and the issue at the heart of the action is one of purity, not inherency.

Applicants further submit that "Fuks et al.'s own inventor admits that its preparation was not pure enough to elicit anti-heparanase antibodies and submit a declaration from Dr. Israel Vlodavsky, filed in the prosecution of a related European case, to support this position.

Applicants argument continues to be acknowledged and has been carefully considered, however, continues to be found non-persuasive on the following basis.

As previously stated, the preparation taught by Fuks et al. is that of an isolated heparanase, from the same source as applicants claimed heparanase and thus Fuks et al. continues to anticipate applicants claimed isolated heparanase protein for all of the reasons of record. Applicants comments that applicants are not (merely) claiming "an isolated heparanase" but rather a heparanase protein "that is pure enough to elicit anti-heparanase antibodies" is acknowledged and it continues to be the position of the office that the "heparanase" protein taught by Fuks et al., as well as the preparation/composition taught by Fuks et al. "is pure enough to elicit anti-heparanase antibodies" even if the heparanase protein taught by Fuks et al. "did not elicit anti-heparanase antibodies" in the referred to procedures/experiments, as described in applicants declarations. The limitation/characteristic that the heparanase, or preparation of the claimed invention "is pure enough to elicit anti-heparanase antibodies" is an inherent limitation/characteristic of the isolated heparanase taught by Fuks et al. as well as the preparation/composition taught by Fuks et al.

It is further noted that applicants submit that the declaration of Dr. Iris Pecker gives two reasons why it would be unobvious to make the preparation of Fuks pure enough to elicit anti-heparanase antibodies. As the current rejection is based upon anticipation and not obviousness, while applicant's comments are acknowledged, they are not found persuasive in overcoming the rejection based on anticipation.

Thus claims 97-101 and 130-133 remain anticipated by Fuks et al.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
3/29/2007